

NOV 18 2005

FAX TRANSMISSION**MS PCT****DATE:** November 18, 2005**PTO IDENTIFIER:** Application Number 10/541,513

Patent Number

Inventor: Sabine Steiger, et al.**MESSAGE TO:** US Patent and Trademark Office**FAX NUMBER:** (571) 273-8300**FROM:** CONNOLLY BOVE LODGE & HUTZ LLP

Roberte M. D. Makowski, Ph.D.

PHONE: (302) 658-9141**Attorney Dkt. #:** 12810-00106-US**PAGES (Including Cover Sheet):** 11**CONTENTS:** Transmittal of Translation of International Preliminary Examination Report(1 page)
Translation of International Preliminary Examination Report (8 pages)
Certificate of Transmission (1 page)

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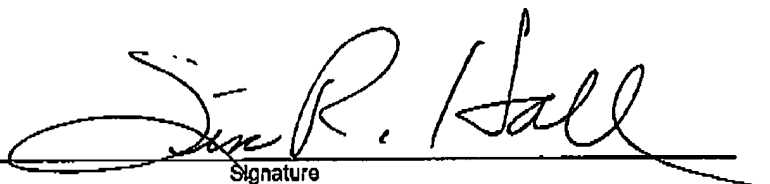
Application No. (if known): 10/541,513

Attorney Docket No.: 12810-00106-US

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Transmittal of Translation of International Preliminary Examination Report
(1 page)

Translation of International Preliminary Examination Report (8 pages)

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NOV 18 2005

Docket No. 12810-00106-US
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:

STEIGER, et al.

Conf. No.: N/A

Application No.: 10/541,513

Group Art Unit: N/A

Filed: July 8, 2005

Examiner: Not Yet Assigned

For: METHOD FOR PRODUCING
KETOCAROTENOIDS BY CULTIVATING
GENETICALLY MODIFIED ORGANISMS

**TRANSMITTAL OF TRANSLATION OF INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

MS PCT
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

Applicants enclose herewith the Translation of the International Preliminary Examination Report.

Applicants believe no fee is due with this communication. However, if a fee is due, the Director is hereby authorized to charge any deficiency in the fees filed, asserted to be filed or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to our Deposit Account No. 03-2775, under Order No. 12810-00106-US, from which the undersigned is authorized to draw.

Respectfully submitted,

By Roberte M. D. Makowski
Roberte M. D. Makowski, Ph.D.

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Patente, Marken u. Lizenzen From the INTERNATIONAL BUREAU

06. Sep. 2005

PCT

NOTIFICATION OF TRANSMITTAL
OF COPIES OF TRANSLATION
OF THE INTERNATIONAL PRELIMINARY REPORT
ON PATENTABILITY
(CHAPTER I OR CHAPTER II
OF THE PATENT COOPERATION TREATY)
(PCT Rule 72.2)

To:

BASF AKTIENGESELLSCHAFT
67056 Ludwigshafen
ALLEMAGNE

AST

Date of mailing (day/month/year)
01 September 2005 (01.09.2005)

Applicant's or agent's file reference
0000054221

IMPORTANT NOTIFICATION

International application No.
PCT/EP2003/014876

International filing date (day/month/year)
24 December 2003 (24.12.2003)

Applicant

BASF AKTIENGESELLSCHAFT et al

1. Transmittal of the translation to the applicant.

The International Bureau transmits herewith a copy of the English translation made by the International Bureau of the international preliminary examination report established by the International Preliminary Examining Authority.

2. Transmittal of the copy of the translation to the elected Offices.

The International Bureau notifies the applicant that copies of that translation have been transmitted to the following elected Offices requiring such translation:

AZ, CA, CH, CN, GH, KG, KP, KR, MK, MZ, RU, TM

The following elected Offices, having waived the requirement for such a transmittal at this time, will receive copies of that translation from the International Bureau only upon their request:

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3. Reminder regarding translation into (one of) the official language(s) of the elected Office(s).

The applicant is reminded that, where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report.

It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned (Rule 74.1). See Volume II of the PCT Applicant's Guide for further details.

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Authorized officer

Yolaine Cussac

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PATENT COOPERATION TREATY



Translation

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 0000054221	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/EP2003/014876	International filing date (day/month/year) 24 December 2003 (24.12.2003)	Priority date (day/month/year) 09 January 2003 (09.01.2003)
International Patent Classification (IPC) or national classification and IPC C12N 9/00, 9/02, C12P 23/00, C12N 5/04		
Applicant BASF AKTIENGESELLSCHAFT		

<p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of <u>8</u> sheets, including this cover sheet.</p> <p><input type="checkbox"/> This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of _____ sheets.</p>
<p>3. This report contains indications relating to the following items:</p> <p>I <input checked="" type="checkbox"/> Basis of the report</p> <p>II <input type="checkbox"/> Priority</p> <p>III <input type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</p> <p>IV <input checked="" type="checkbox"/> Lack of unity of invention</p> <p>V <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p>VI <input type="checkbox"/> Certain documents cited</p> <p>VII <input type="checkbox"/> Certain defects in the international application</p> <p>VIII <input type="checkbox"/> Certain observations on the international application</p>

Date of submission of the demand 01 July 2004 (01.07.2004)	Date of completion of this report 14 April 2005 (14.04.2005)
Name and mailing address of the IPEA/EP	Authorized officer
Facsimile No.	Telephone No.

Form PCT/IPEA/409 (cover sheet) (July 1998)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/EP2003/014876

I. Basis of the report

1. With regard to the elements of the international application:*

- ☒ the international application as originally filed
- ☒ the description:
pages 1-43, as originally filed
pages, filed with the demand
pages, filed with the letter of
- ☒ the claims:
pages 1-43, as originally filed
pages, as amended (together with any statement under Article 19
pages, filed with the demand
pages, filed with the letter of
- ☒ the drawings:
pages 1/3-3/3, as originally filed
pages, filed with the demand
pages, filed with the letter of
- ☒ the sequence listing part of the description:
pages 1-15, as originally filed
pages, filed with the demand
pages, filed with the letter of

2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language _____ which is:

- ☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of the translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☒ contained in the international application in written form.
- ☒ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☒ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☒ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:

- ☐ the description, pages _____
- ☐ the claims, Nos. _____
- ☐ the drawings, sheets/fig. _____

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rule 70.16 and 70.17).

** Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.

Form PCT/IPEA/409 (Box I) (July 1998)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/EP2003/014876

IV. Lack of unity of invention

1. In response to the invitation to restrict or pay additional fees the applicant has:

- ☐ restricted the claims.
- ☐ paid additional fees.
- ☐ paid additional fees under protest.
- ☐ neither restricted nor paid additional fees.

2. ☒ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

- ☐ complied with.
- ☐ not complied with for the following reasons:

4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:

- ☒ all parts.
- ☐ the parts relating to claims Nos. _____

Form PCT/IEPA/409 (Box IV) (July 1998)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP 03/14876
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Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of IV.

Unity of the invention (PCT Rule 13)

As a result of the assessment of inventive step, the examiner is of the opinion that the claimed subject matter of the present application lacks unity.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

 International application No.
 PCT/EP 03/14876

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	1-43	YES
	Claims		NO
Inventive step (IS)	Claims		YES
	Claims	1-43	NO
Industrial applicability (IA)	Claims	1-43	YES
	Claims		NO

2. Citations and explanations

The subject matter of the present application

Method of producing ketocarotinoids by cultivating genetically modified microorganisms or plants with increased ketolase activity characterized in that the modification is brought about by the expression of a ketolase with SEQ. ID. NO. 2 or a ketolase derived therefrom.

Cited documents (PCT Rule 64(1))

- D1: EP-A-O 735 137
 D2: WO 99/07867 A
 D3: WO 99/61652 A
 D4: MEEKS ET AL. (2001) PHOTOSYNTHESIS RES. 70, 85-106
 D5: WO 03/012056 A
 D6: WO 03/080849 A
 D7: WO 2004/018693 A
 D8: WO 2004/018694 A
 D9: DE 102 38 978 A
 D10: KANEKO ET AL (2001) DNA RESEARCH 8, 205-213
 D11: MOFFITT ET AL. (2003) J. MOL. EVOL. 56, 446-457
 D12: MISAWA ET AL. (1998) J. BIOTECHNOL. 59, 169-181
 D13: LEE ET AL. (2002) APPL MICROBIOL BIOTECHNOL. 60, 1-11
 D14: SIEIRO ET AL (2003) INT. MICROBIOL 6, 11 -16
 D15: MISAWA ET AL. (1995) J. BACT. 22, 6575-6584

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/EP 03/14876

D5-D9, D11 and D14 are not regarded as prior art under PCT Rule 64(1).

Novelty (PCT Article 33(2))

D1 to D3 and the documents cited on page 3 (lines 1-18) of the description are considered to be the closest prior art. These documents disclose the production of ketocarotinoids using genetically modified organisms (microorganisms and plants) by increasing the ketolase activity. However, the disclosed ketolases have only very little identity with the ketolase of SEQ. ID. NO. 2.

D4 discloses the genomic sequence of the cyanobacteria *Nostoc punctiforme* (see also "<http://genome.ornl.gov/microbial/npun>").

The prior art citations D10 and D11 disclose the sequences of two ketolases (EBI:Q8YSA0 (D10); EBI: Q847D1 (D11)). The ketolase of D10 has an identity of 56% with SEQ. ID. NO. 2 and 59% with SEQ. ID. NO. 4. The presumed ketolase of D11 has an identity of 62% with SEQ. ID. NO. 2 and 79% with SEQ. ID. No. 4.

D12-D14 describe the production of carotinoids using genetically modified microorganisms.

Conclusion: The subject matter of claims 1 to 43 is novel.

Inventive step (PCT Article 33(3))

The closest prior art is D1 to D3.

Thus the problem to be solved by the present application can be regarded as that of providing an alternative ketolase.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/EP 03/14876

The applicant's solution for providing a ketolase with SEQ. ID. NO. 2 or a ketolase derived therefrom currently does not appear to be inventive for two reasons.

- 1) The examiner is of the opinion that any ketolase solves the problem. In light of the fact that: i) it was known that some cyanobacteria synthesize ketocarotenoids, and ii) the genomic sequence of one of these cyanobacteria was known, it was obvious for a person skilled in the art to identify sequences from these cyanobacteria which are homologous with crtW or crtO and to use them as alternatives. Consequently, an inventive step could be recognized only if direct comparative experiments were provided and unexpected effects present.
- 2) The lower limit of the identity of the derived ketolases (42%) appears to be selected only to: i) establish novelty over, for example, crtW or crtO, and ii) establish unity between SEQ. ID. NO. 2 and 4 (53% identical), but not to support experimental values. Consequently, this feature cannot be taken into account for the assessment of inventive step. Since this is apparently a new group of ketolases, a lower identity limit of 70-75% would appear to be acceptable.

The additional features in the dependent claims are known to a person skilled in the art.

An inventive step therefore currently cannot be recognized for claims 1 to 43.

Industrial applicability (PCT Article 33(4))

The subject matter of claims 1 to 43 is industrially applicable.